ASN Kidney Health Guidance

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ASN Kidney Health Guidance on the Management of Obesity in Persons Living with Kidney Diseases

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Introduction

Obesity is an expanding public health threat, which heightens risk of multiple chronic diseases, including kidney diseases. Within the past two decades, the percentage of US adults with a body mass index (BMI) ≥30 kg/m^2 has increased from 30.5% to 41.9%. Obesity is categorized into three classes with class 1, 2, and 3 defined as a BMI 30–34.9, 35–39.9, and ≥40 kg/m^2, respectively. The incidence of Class 3 obesity (BMI ≥40 kg/m^2) is now increasing faster than other classes (and has almost doubled from 4.7% to 9.2%).[1] The adverse effect of obesity on disease progression is not limited to kidney disease associated with type 2 diabetes but also includes monogenic kidney diseases, such as polycystic kidney disease[2] and glomerular diseases.[3–7] Obesity, particularly severe obesity, often precludes access to kidney transplantation.[8]

For the patient living with both obesity and kidney diseases, weight loss can improve psychosocial functioning, including better mood; heighten quality of life; and slow kidney disease progression.[9–11] Effective management of obesity in patients with kidney diseases remains challenging and requires a multidisciplinary team that includes kidney health professionals. Obesity can be treated with lifestyle modifications, such as diet; however, fewer than one in four adults who achieve substantial weight loss with lifestyle intervention sustain the weight loss.[12,13] Advancements in tools to treat obesity, including antiobesity medications (AOMs) and metabolic and bariatric surgery, now allow lifestyle modification to complement alternative interventions to induce and sustain weight loss (Figure 1).

In light of these data, the American Society of Nephrology (ASN) recommends that nephrologists and other kidney health professionals understand the tools and interventions available to help adults with obesity and kidney diseases safely lose weight. To improve kidney and metabolic health as well as overall quality of life, ASN formed an expert workgroup to develop guidance for the management of obesity in patients with kidney diseases under the direction of the ASN Kidney Health Guidance (KHG) oversight committee. This ASN KHG provides nephrologists and other kidney health professionals with knowledge on the existing tools for obesity management and guidance on implementation of these tools within clinical practice on the basis of best available evidence and expert opinion. Describing an ideal framework with an underpinning of the importance of psychosocial aspects of care to support medical interventions (*e.g.*, lifestyle modifications and pharmacological interventions), this guidance requires a multidisciplinary kidney care team for optimization of outcomes. The kidney community, in

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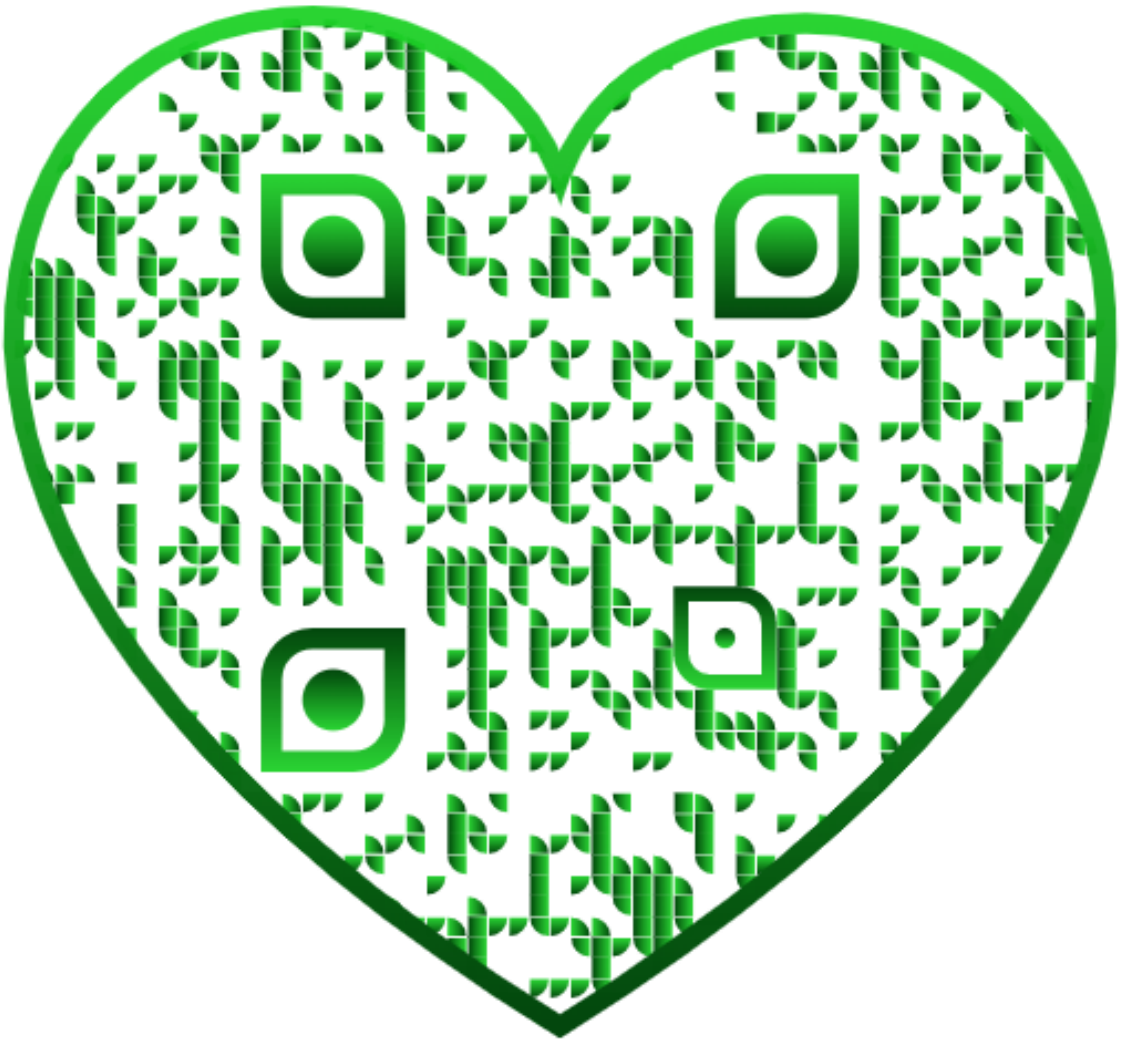

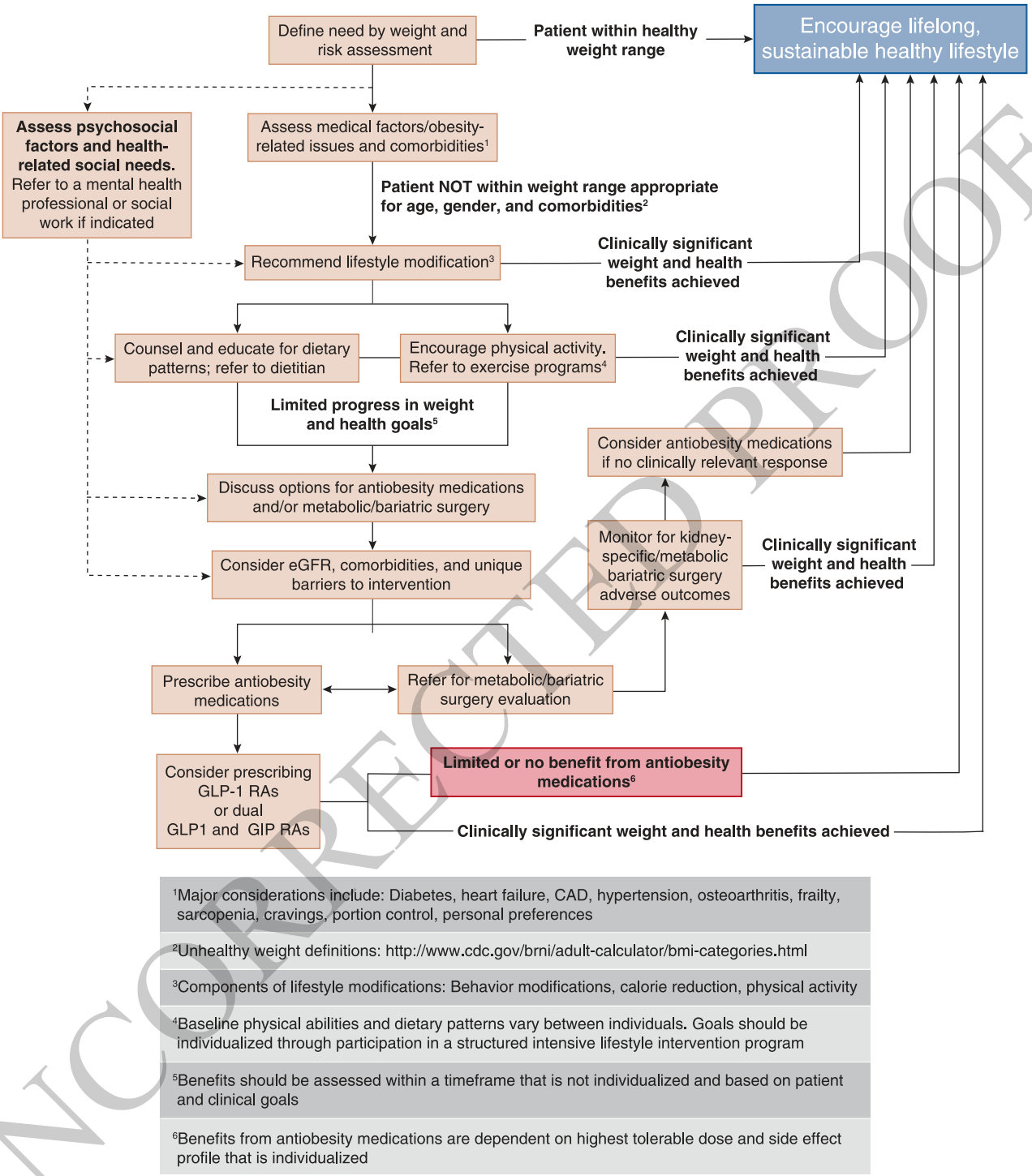
Define need by weight and risk assessment
Patient within healthy weight range
Encourage lifelong, sustainable healthy lifestyle
Assess psychosocial factors and health-related social needs. Refer to a mental health professional or social work if indicated
Assess medical factors/obesity-related issues and comorbidities[1]
Patient NOT within weight range appropriate for age, gender, and comorbidities[2]
Recommend lifestyle modification[3]
Clinically significant weight and health benefits achieved
Counsel and educate for dietary patterns; refer to dietitian
Encourage physical activity. Refer to exercise programs[4]
Clinically significant weight and health benefits achieved
Limited progress in weight and health goals[5]
Consider antiobesity medications if no clinically relevant response
Discuss options for antiobesity medications and/or metabolic/bariatric surgery
Monitor for kidney-specific/metabolic bariatric surgery adverse outcomes
Clinically significant weight and health benefits achieved
Consider eGFR, comorbidities, and unique barriers to intervention
Prescribe antiobesity medications
Refer for metabolic/bariatric surgery evaluation
Consider prescribing GLP-1 RAs or dual GLP1 and GIP RAs
Limited or no benefit from antiobesity medications[6]
Clinically significant weight and health benefits achieved
[1]Major considerations include: Diabetes, heart failure, CAD, hypertension, osteoarthritis, frailty, sarcopenia, cravings, portion control, personal preferences
[2]Unhealthy weight definitions: http://www.cdc.gov/brni/adult-calculator/bmi-categories.html
[3]Components of lifestyle modifications: Behavior modifications, calorie reduction, physical activity
[4]Baseline physical abilities and dietary patterns vary between individuals. Goals should be individualized through participation in a structured intensive lifestyle intervention program
[5]Benefits should be assessed within a timeframe that is not individualized and based on patient and clinical goals
[6]Benefits from antiobesity medications are dependent on highest tolerable dose and side effect profile that is individualized

Figure 1. Unhealthy weight treatment algorithm. The unhealthy weight treatment algorithm depicts an ideal framework to support clinical decision making for the management of unhealthy weight in adults 18 years and older living with kidney diseases. GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like protein-1 receptor agonist.

partnership with ASN, can work toward advocating for policy, reimbursement, and infrastructure changes to support this ideal model.

This KHG focuses on adults 18 years and older living with obesity and kidney disease. The intended audience includes all kidney health professionals who work within a kidney health care team, including nephrologists, nurses, dietitians, advanced practice professionals, and social workers along with primary care physicians, obesity medicine and metabolic/bariatric surgery specialists, endocrinologists, and policymakers. A theme throughout this guidance is that obesity requires a team-based approach and a combination of multiple interventions to achieve and sustain safe weight loss.

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Psychosocial Considerations for the Management of Persons Living with Obesity and Kidney Disease

To effectively treat obesity, clinicians should support patients by addressing health-related social needs and identifying and treating common mental health comorbidities. Clinicians should use shared decision making when selecting treatment options and counsel patients with sensitivity and consideration of their prior experiences of trauma, racism, discrimination, and weight bias.

Health-Related Social Needs

Health-related social needs (*i.e.*, social determinants or drivers of health) contribute to approximately half of the observed variation in health outcomes across the United States.[14,15] Food and nutrition insecurity, housing insecurity, health literacy, and economic and transportation instability can interfere with the effective treatment of obesity and chronic diseases, including kidney diseases, and impede access to nutritious foods, medications, and health care.[16] Supplemental Table 1 highlights health-related social needs screening resources and referral options.

Mental and Behavioral Health

Obesity and its associated comorbidities are often compounded by a substantial psychosocial burden for many, but not all, individuals. Current research in this space has focused primarily on psychopathology—diagnoses including mood and anxiety disorders, eating disorders, and substance use disorders. Other studies have focused on life experiences and psychosocial issues that may contribute to the patient's motivation for seeking metabolic/bariatric surgery for obesity treatment.

Much of the research on the relationship between psychiatric diagnoses and obesity comes from patients with more severe forms of obesity and those treated with metabolic/bariatric surgery. Mood disorders, including major depressive disorder and bipolar disorder, are diagnosed in up to 32% of candidates for surgery while up to 24% are diagnosed with an anxiety disorder.[17] Binge eating disorder, characterized by recurrent (≥2 days/wk for 6 months) episodes of binge eating episodes during which individuals experience a loss of control over their eating, can be seen in up to 15% of patients. Importantly, up to 36% of patients with more severe forms of obesity who present for metabolic/bariatric surgery report a lifetime history of substance use disorders, representing an important opportunity for screening and intervention.[18]

A range of life experiences and psychosocial issues likely influence the decision to seek weight loss interventions. Many patients with obesity report low self-esteem and greater body image dissatisfaction than those persons with a lower BMI. Persons with more severe forms of obesity often report poor physical functioning, such as walking or climbing stairs, which can impede employment and also increase the need for medical disability.

Stigmatization of Patients with Obesity and Kidney Diseases

Persons with obesity are frequently stigmatized, if not subjected to discrimination in many settings, including educational, employment, and medical settings, which may lead to avoidance of clinical care and worse health outcomes.[19] Weight stigma and internalized weight bias, in which individuals apply negative beliefs about body weight to themselves, are associated with negative mental health outcomes and, in some cases, worse physical health outcomes.[20]

Kidney health care professionals must be sensitive to weight stigma when communicating about obesity. Effective patient–provider conversations should be centered on holistic health and quality-of-life considerations and patient motivations, goals, and barriers for weight loss. Health care professionals should reflect on their own biases regarding weight and use terms such as "unhealthy weight" versus calling patients "fat" or "obese."[21] While clinicians may avoid conversations about obesity because of concerns of patient embarrassment, patients commonly report a desire for more engagement with their clinicians about obesity, including helping them disentangle conflicting nutritional advice, select goals and treatment, and follow-up on success.[22,23] Clinicians should advocate for training on obesity management, adequate clinic time to address obesity, and establishment of interdisciplinary care teams to best facilitate comprehensive person-centered weight management.

Most patients experience profound improvements in psychosocial functioning with weight loss. On the other hand, after weight loss, some patients may struggle with maintaining weight loss and/or experience depression and self-injurious behavior, substance abuse, body image dissatisfaction, and experience difficulties with romantic relationships. All care team members should be aware of these potential complications and refer patients for additional mental health assessment and treatment if warranted. Preferably, nephrology clinics should have ready access to a mental health professional who can assess mental health, help determine appropriateness of obesity treatments, and provide support during and after obesity treatment.

Lifestyle Modification and Weight Loss

Lifestyle modification includes long-term adjustments in dietary intake, physical activity, and other daily habits.[24] It is first-line therapy for weight management because it is a safe, noninvasive, and potentially sustainable way to treat obesity and its associated comorbidities and improve overall health. Lifestyle modifications, such as whole-food plant-dominant diet, portion control, mindfulness, physical activity on most days, stress reduction, and adequate sleep, serve as the foundations to long-term weight loss success. Individuals with obesity should be provided education and support to implement lifestyle modifications regardless of use of other therapeutic options to manage obesity.

Efficacy of Lifestyle Modification on Weight Management in Persons Living with Kidney Diseases

The cumulative weight loss benefit and durability from lifestyle modification are variable. The interaction of several individual-level factors (*e.g.*, age, sex, comorbidities, and psychosocial circumstances) and environmental factors contribute to a person's ability to lose weight. Physical

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activity combined with dietary change leads to more sustained weight loss than dietary change alone.[25,26] Clinical practice guidelines for the evaluation and management of kidney diseases recommend that adults with kidney diseases engage in at least 150 minutes of moderate intensity physical activity per week[27] and guidelines for management of obesity in adults recommend 200–300 minutes or more per week to prevent weight regain after intentional weight loss.[28,29] Baseline physical abilities and dietary patterns vary between individuals, but success can be augmented through participation in a structured intensive lifestyle intervention program, which consists of multiple sessions with a health care professional to establish goals, identify barriers to behavior change, problem solve, and track progress.

Facilitating behavioral modification is a critical aspect of obesity treatment that incorporates strategies from cognitive behavioral therapy to address thinking patterns and motivational issues. Although time is limited during nephrology visits and/or providers may lack relevant training or experience, providers may practice a few strategies highlighted in Table 1 and apply to patient encounters to identify barriers and individualize counseling.

Comprehensive lifestyle intervention programs can, in some individuals, be effective in achieving clinically significant weight loss of ≥5% of initial body weight; improving glycemic, anthropometric[30] and cardiometabolic measures; and reducing incidence of very high-risk kidney disease in people with type 2 diabetes.[31] Scheduling regular and frequent follow-up visits to review health goals, strategize to overcome barriers, and track progress is recommended to increase likelihood of weight loss success.[32] By contrast, weight loss success does not vary widely between dietary approaches.[33,34]

Translating results from weight management studies to people living with kidney diseases is challenging because of low representation of this population in clinical studies. Furthermore, evaluation of long-term weight loss durability is limited because of a follow-up of ≤3 years in most studies.[35,36] Observational weight loss studies using a variety of diets, exercise training, or a combination of exercise and diet have demonstrated that people with kidney disease stages 1–4 can lose a substantial amount of weight and maintain this weight loss for up to 24 months, but whether these results can be extrapolated to individuals with more advanced kidney diseases remains untested. Lifestyle interventions may lead to improvements in BP, physical function, and other markers of health independent of weight loss.

Safety Considerations

Nonserious adverse events, including musculoskeletal concerns (pain, fatigue, *etc.*), may occur with lifestyle interventions, but serious adverse events seem to be rare, even in people with kidney diseases.[37,38] Safety may be improved by following current clinical guidelines related to nutrition and physical activity in kidney diseases,[27,28,39,40] such as when discussing diets that may contain high levels of protein and certain electrolytes like potassium or phosphorus. Consultation with professionals, such as registered dietitians and exercise physiologists, can help ensure the safety and effectiveness of lifestyle changes.

Table 1. Core skills to facilitating behavioral modification skills

Core Skills	Components
Self-monitoring	• Daily recording of food intake • Daily or weekly exercise tracking • Regular self-weighing
Goal setting	• Set specific, measurable, achievable, relevant, and time-bound goals in collaboration with a clinician • Progress assessment at follow-up visits
Stimulus control	• Self-identification of environmental cues triggering unhealthy eating and low physical activity • Create an environment that makes healthy behaviors the default
Problem solving	• Identify a problem in detail • Create potential solutions • Consider the pros and cons of each option • Choose a solution • Develop an implementation plan • Evaluate the effectiveness of the chosen solution once the behavior has been implemented

Goals of Care

Transplant centers should consider referral for obesity evaluation and treatment for any individual who is specifically not waitlisted or denied kidney transplantation because of a BMI cutpoint, which could be center specific. Health and weight goals should be individualized and aim for sufficient weight loss to facilitate kidney transplant waitlisting. Weight loss interventions may also delay or prevent kidney failure and/or cardiovascular disease by stabilization or improvement in kidney function, albuminuria, glucose control, and/or BP. Early ascertainment of these weight management goals and revisiting goals at each visit is vital to ensure the anticipated treatment outcome aligns with the person's health objectives and needs. If weight loss goals are not achieved with a 3–6-month trial of lifestyle modifications or within a time frame that is individualized and based on the patient and clinical goals, clinicians may consider adding pharmacotherapy or metabolic/bariatric surgery, especially for those who report challenges adhering to nutrition and physical activity changes.

Pharmacologic Options

Accumulating evidence suggests that AOMs may be safe and beneficial for people living with obesity and kidney diseases.

US Food and Drug Administration–Approved AOMs

Multiple aspects should be considered for a comprehensive approach to counsel patients on US Food and Drug Administration (FDA)-approved classes of AOMs (Table 2). Incretin mimetics, specifically glucagon-like protein-1 receptor agonists (GLP-1 RA) and glucose-dependent insulinotropic polypeptides (GIPs), represent the most effective and beneficial medications for managing obesity in persons with kidney diseases because of their cardiovascular, kidney, metabolic, and survival benefits. However, other

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Table 2. Pharmacologic options for the treatment of obesity in persons with kidney diseases

Drug	FDA Indications and Dosage[a]		Total Expected % Weight Loss	Evidence in Kidney Diseases	Beneficial Outcomes[b]	Adverse Effects, Contraindications and Warnings[a]
	Weight Loss Max Dose	Renal Dose Range				
Incretin mimetics (GLP-1 RAs and/or GIP)						
Tirzepatide[41,42]	15 mg weekly	Starting dose: 2.5 mg/wk Max dose: 15 mg/wk	Mean 20.9% weight loss in the 15-mg group	18% of patients in SURPASS-4 had eGFR <60	Kidney:[c] Heart:[c] Survival:[c]	Adverse effects: Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase, gallbladder disease Warnings and precautions: thyroid C-cell tumors (in rodents), pancreatitis, hypoglycemia (with insulin secretagogue) Contraindications: personal or family history of medullary thyroid cancer, MEN syndrome type 2, known hypersensitivity to drug, pregnancy
Liraglutide[43–45]	3 mg daily	Starting dose: 0.6 mg/d Max dose: 3 mg/d	Mean 8%	Approximately 20% of patients in LEADER with eGFR <60, including 2.4% with eGFR <30	Kidney:[d] Heart:[d] Survival:[d]	
Semaglutide (subQ)[46–49]	2.4 mg weekly (max dose in FLOW was 1.0 mg.)	Starting dose: 0.25 mg/wk Max dose: 2.4 mg/wk	Mean 12.4%	STEP 1–3 included approximately 30% of patients with eGFR <90 FLOW included patients with eGFR 25–75 (n=3533)	Kidney:[d] Heart:[d] Survival:[d]	
Semaglutide (oral)[e,50,51]	n/a	Starting dose: 3 mg daily Max dose: 14 mg daily	Mean 3.0% weight loss	PIONEER 5 included patients with eGFR 30–59 (N=324)	Kidney:[d] Heart:[d] Survival:[d]	
Dulaglutide[e,52]	n/a	Starting dose: 1.5 mg/wk Max dose: 4.5 mg/wk	Mean 3%–5%	AWARD 7 included 577 patients with stage 3–4 CKD	Kidney:[d] Heart:[d] Survival:[c]	
Opioid receptor antagonist						
Naltrexone/bupropion[53]	32/360 mg	Starting dose: 8/90 mg Max dose: 8/90 mg twice a day	More than 5% weight loss in approximately 40% of participants	Contraindicated in ESKD	Kidney:[c] Heart:[c] Survival:[c]	Adverse effects: may exacerbate depression, seizure disorder, and hypertension Warning and precautions: severe liver disease/ESKD—not recommended Contraindications: ESKD
Antiobesity medication						
Orlistat[54]	120 mg three times daily	120 mg three times daily	Mean approximately 3%	Limited data. As the drug is minimally absorbed, no dosage adjustment is needed in CKD	Kidney:[c] Heart:[c] Survival:[c]	Adverse effects: oily spotting, flatus with discharge, fecal urgency fatty/oily stool, fecal incontinence Warnings/precautions: advise patients take nutritionally balanced, reduced-calorie diet (30% fat), multivitamin with fat-soluble vitamin at least 2 h before or after orlistat. Cyclosporine administer 3 h afterward, levothyroxine at least 4 h apart Decreased cyclosporine exposure, increased urinary oxalate, rare cases severe liver injury, monitor renal function in patients at risk of renal insufficiency Contraindications: pregnancy, chronic malabsorption syndrome, cholestasis, known hypersensitivity

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Table 2. Continued

Drug	FDA Indications and Dosage[a]		Total Expected % Weight Loss	Evidence in Kidney Diseases	Beneficial Outcomes[b]	Adverse Effects, Contraindications and Warnings[a]
	Weight Loss Max Dose	Renal Dose Range				
Stimulants						
Phentermine/topiramate [55,56]	15/92 mg	Starting dose: 3.75/23 mg Max dose: 7.5/46 mg	Mean 10.9%	−7.9% (for 7.5/46 mg dose, not specific to kidney disease pts −8.1/102.6 kg)	Kidney:[c] Heart:[c] Survival:[c]	Adverse effects: reduced concentration, word-finding difficulty, irritability, dry mouth, kidney stones, palpitations, modest increase in BP, hypokalemia, metabolic acidosis, and nephrolithiasis Warnings and precautions: consider alternative antiobesity medication for patients with metabolic acidosis, nephrolithiasis, or hypokalemia before initiation of phentermine-topiramate. Discontinuation of phentermine-topiramate requires dose titration to every other day for 1 wk to avoid risk of withdrawal seizure Contraindications patients who are pregnant, have glaucoma, have hyperthyroidism, or within 14 d after monoamine oxidase inhibitor use

FDA, US Food and Drug Administration; FLOW, Evaluate Renal Function with Semaglutide Once Weekly; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like protein-1 receptor agonist; MEN, multiple endocrine neoplasia.
[a]Verify dosage considerations for other comorbid conditions using the respective package insert.
[b]See Supplemental Table 2 for data detailing summary of outcomes.
[c]Indicates a lack of data or lack of conclusive evidence regarding benefit.
[d]Indicates positive benefits found in clinical trials.
[e]Not US Food and Drug Administration approved for weight loss indication as of June 30, 2024.

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AOMs are available that are safe for patients with kidney diseases stage 1–3b but may require dose adjustment in patients with more advanced kidney disease.

Incretin Mimetics (GLP-1 RAs and Dual GLP-1/GIP RAs)

The landscape of pharmacological therapy in kidney diseases is rapidly evolving with several agents, in particular GLP-1 RAs. As of August 16, 2024, 3 GLP-1 RAs are approved specifically for weight loss regardless of diabetes status: liraglutide, tirzepatide, and semaglutide. Weight loss in the GLP-1 RA class often exceeds 5% of baseline body weight, although degree of weight loss is variable depending on the drug, dosage, study population, and whether intensive lifestyle counseling was provided (see Table 2 and Supplemental Table 2 for key GLP-1 RA data). In the Evaluate Renal Function with Semaglutide Once Weekly trial designed to examine the effect of semaglutide on kidney disease outcomes in patients with type 2 diabetes and albuminuria (eGFR 25–75), semaglutide reduced the risk of major kidney disease outcomes by approximately 25%.[46] A prespecified analysis of the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity cardiovascular outcomes trial in adults without preexisting cardiovascular disease and BMI ≥27 kg/m^2, semaglutide 2.4 mg subcutaneous weekly administration showed a reduction on a five-component kidney composite end point by 22%, although this was largely driven by effect on albuminuria. Rate of eGFR decline was 0.75 ml/min per 1.73 m^2 lower in the GLP-1 versus placebo group at 104 weeks.[48] In a *post hoc* analysis of the RCT of tirzepatide versus insulin glargine, tirzepatide decreased albuminuria, slope of eGFR decline and a composite of four-component kidney composite end point.[42] Similarly, an RCT with liraglutide (1.8 mg SQ daily) demonstrated a 22% lower occurrence of composite renal outcome versus placebo and was primarily driven by the reduction of new onset of persistent microalbuminuria.[43]

When prescribing incretin mimetics, clinicians should be aware of specific contraindications and counsel patients on expected adverse effects. Incretin mimetics should be initiated at the lowest dose and titrate up gradually. Although package inserts provide weekly or monthly titration schedules, prescribers can opt to maintain a dose while individuals work on lifestyle modifications and then increase the dose when weight loss plateaus. To mitigate gastrointestinal symptoms, patients should be advised to consume small meals slowly and to avoid high-fat, calorie-dense foods. If significant nausea, indigestion, constipation, or diarrhea occurs, prescribers should assess dietary quality and quantity and elucidate behaviors that promote reflux, such as large portion size, rapid meal consumption (<20 minutes), and lying down <2 hours after eating. If modifications in diet or behavior do not improve symptoms, then a stepwise dose reduction to the last tolerable dose is recommended. However, persistent abdominal pain and/or vomiting may indicate pancreatitis, cholelithiasis, or cholestasis. In these situations, prescribers should discontinue incretin mimetics immediately and assess for kidney and electrolyte abnormalities, transaminitis, or elevated lipase or amylase levels. Imaging with ultrasound or computed tomography scan may be warranted if initial screening is positive. Reinitiation of incretin mimetics may be considered if there is no diagnosis of serious medication-related adverse effects.

GLP-1 RAs can increase hypoglycemia risk when used in combination with sulfonylureas or insulin. If blood glucose is well controlled, the basal insulin dose may need to be reduced by 10%–20% with ongoing glucose monitoring and close multidisciplinary collaboration. Patients should self-monitor BP because weight loss and reduced dietary salt intake may necessitate decreasing antihypertensive treatment.[57]

Opioid Receptor Antagonists

Naltrexone (an opioid receptor antagonist) combined with bupropion (a dopamine and norepinephrine reuptake inhibitor) suppresses appetite and promotes weight loss. Because of the lack of data on the safety and efficacy of this agent in kidney diseases, presence of uncontrolled hypertension or ESKD is an absolute contraindication for its use.

Orlistat

Orlistat inhibits hydrolysis of triglycerides, resulting in reduced absorption of free fatty acids and approximately 3% weight loss. Because of its mechanism, orlistat can increase urine oxalate levels, and its use is often limited in clinical practice because of gastrointestinal side effects. Its long-term kidney and cardiovascular disease outcomes have not been studied thoroughly.

Phentermine/Topiramate

The combined formulation of phentermine and topiramate suppress appetite and promotes weight loss. Dose adjustment according to kidney function is necessary, and the drug should be avoided in advanced kidney diseases. The effect of phentermine/topiramate on kidney outcomes and cardiovascular morbidity and mortality has not been established.

Medications with Some Weight Loss Benefit But Not FDA Approved for This Indication

Metformin

Metformin use shows modest short-term weight lowering and long-term weight maintenance effects. Metformin's mechanism on weight reduction is unclear, but may be related to improvements in insulin sensitivity, inhibition of gluconeogenesis, and effects on gut microbiota and the immune system. Metformin is not FDA approved for weight loss, and its off-label use should be disclosed to patients when prescribed for weight management. Prescription of metformin should be limited to patients with eGFR >30 ml/min per 1.73 m^2 to reduce the risk of metformin-associated lactic acidosis. Gastrointestinal side effects, such as diarrhea or bloating, are common but can be minimized by using extended release formulation, dose reduction to once daily, or taking with food.[58–60]

Sodium-Glucose Cotransporter-2 Inhibitors

In addition to having beneficial cardiovascular-kidney-metabolic effects, sodium-glucose cotransporter-2 (SGLT-2) inhibitors shift metabolism to a pseudofasting state

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promoting endogenous glucose production, increased lipolysis, and ketogenesis. In addition, SGLT-2 inhibitors can produce up to 75 g of glucose excretion or approximately 300 calorie loss per day.[61] In diabetes trials, SGLT-2 inhibitors reduce weight by 2.73 kg, with most of the weight loss in the first 4 weeks.[62] Weight loss effects seem more modest in kidney diseases primarily driven by reducing total body water.[63–65]

Metabolic/Bariatric Surgery in Obesity and Kidney Diseases

Metabolic/bariatric surgery, first developed in the 1950s, remains the most durable and effective intervention for the treatment of obesity. Very few randomized trials of metabolic/bariatric surgery have included individuals with kidney diseases, but high-quality evidence from existing trials and follow-up data of large cohorts of adults suggest that these procedures are safe and effective, and kidney diseases should not be considered a contraindication. However, patients with advanced kidney diseases and those treated with dialysis have higher mortality and complication rates after metabolic/bariatric surgery than those with earlier stages or no kidney disease. Absolute mortality rates with metabolic/bariatric surgery are very low regardless of kidney disease stage,[66] and selection and optimization of patients by a multidisciplinary team may help to mitigate risks associated with metabolic/bariatric surgery.[67] Metabolic/bariatric surgery can be complicated by AKI, hyperoxaluria, kidney stones, and surgical complications (Supplemental Table 3). The risk of postsurgical complications should be discussed with patients when determining referral for metabolic/bariatric surgery.

Considerations for Metabolic/Bariatric Surgery Candidacy in Patients with Kidney Diseases

Patients with severe or uncontrolled psychiatric disorders, eating disorders, or active substance use disorders are not considered good candidates for metabolic/bariatric surgery. Special considerations should be given to comorbid conditions that increase operative risk, including established cardiovascular disease, uncontrolled hypertension, diabetes, and obstructive sleep apnea. Similarly, risk–benefit ratio among older adults with or without frailty should be considered before referring patients for metabolic/bariatric surgery because benefits in this population have not been well established. Upon determination of appropriateness for metabolic/bariatric surgery, patients should be referred to an accredited metabolic/bariatric surgery center (*e.g.*, Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program). In addition to potential eligibility for the procedures, preoperative nutrition counseling should consider the unique dietary and fluid needs of patients with kidney diseases. Patients receiving maintenance dialysis or with advanced kidney disease are often instructed to restrict their fluid intake. Any fluid restrictions may need to be adjusted, especially during the first few months after metabolic/bariatric surgery when solid food intake may not be tolerated.[68]

Benefits and Risks of Metabolic/Bariatric Surgery in Persons Living with Kidney Disease

Bariatric procedures, including intestinal bypass procedures, such as Roux-en-Y gastric bypass, and gastric reduction procedures, such as sleeve gastrectomy, reduce body weight, improve glycemic control, and lower BP, which may reduce risk of kidney disease progression.[69] Bariatric procedures may also benefit the kidneys through alterations in adipokine signaling, such as increasing adiponectin levels (leading to improvement in podocyte effacement and reduction in albuminuria) and reducing leptin levels (resulting in reduction of renin-angiotensin-aldosterone system activation and improved BP control).

Observational studies have reported a lower risk of incident kidney disease (measured using eGFR <60 ml/min per 1.73 m^2 or development of albuminuria) among those undergoing metabolic/bariatric surgery[70,71] and improvement in glomerular hyperfiltration.[72] At the 5-year follow-up of the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently randomized controlled trial (comparing different bariatric procedures with medical therapy), the urine albumin-creatinine ratio was significantly lower in the sleeve gastrectomy group compared with the medical therapy group.[73] Most of these studies examined the changes in kidney function using creatinine-based eGFR, which is likely confounded by loss of lean muscle mass. In addition, previous studies have not compared changes in kidney measures in persons with obesity receiving metabolic/bariatric surgery versus recently FDA-approved GLP-1 RA or GLP-1/GIP RAs, such as semaglutide and tirzepatide.[74]

In adults with non–dialysis-dependent kidney diseases, several observational studies noted lower risk of kidney disease outcome measures, such as >30% decline in eGFR and doubling of serum creatinine and ESKD in obese adults who underwent metabolic/bariatric surgery versus those who did not.[75] One retrospective study (n=425) with 8-year follow-up, which included adults with obesity and kidney disease stages 3–4, reported a 60% lower risk of progression of kidney impairment and a 44% lower risk of kidney failure or death in those who underwent metabolic/bariatric surgery compared with those treated with GLP-1 RA alone[76] (Table 3). Metabolic/bariatric surgery has been prescribed in patients with advanced kidney diseases to improve candidacy for transplantation.[82] Limited studies suggest that more than 50% of patients with ESKD and class 3 obesity can be listed for kidney transplant within 5 years or less after metabolic/bariatric surgery.[80,83]

Following Patients Throughout the Surgical Process

The effect of metabolic/bariatric surgery on kidney function and health can be evaluated by monitoring the serum creatinine level and UPCR/urine albumin-creatinine ratio over time. Because patients may lose muscle mass after bariatric/metabolic surgery and urinary creatinine excretion may subsequently decline, timed urine collections may provide more reliable assessments of change in urinary protein or albumin excretion if urine collection is performed correctly.[27] Monitoring during the early postoperative

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Table 3. Clinical outcomes after metabolic/bariatric surgery in patients with kidney disease

Study	Type of Study/*n*	Baseline GFR or CKD Stage/Albuminuria	Procedure	% Body Weight Lost/Decrease in BMI	Impact on Kidney Function (eGFR, Albuminuria) and Other Clinical Outcomes
Chang *et al.*[77] (United States)	Matched case-control study/1970	eGFR <60: 4.7% eGFR 60–89: 27.5% eGFR >90: 67.8%	Roux-en-Y gastric bypass (96.5%) Sleeve gastrectomy (3.5%)	5 yr: 34.2 kg loss versus 1.3 kg gain in the control group	eGFR decline >30%: HR, 0.46; 95% CI, 0.36 to 0.60 Doubling of serum creatinine or ESKD: 0.49 (0.30 to 0.82)
Liakopuolos *et al.*[78] (Sweden)	Matched case-control/10642	eGFR: 99.4 (17.6) in the surgery group Albuminuria: 26.8%	Roux-en-Y gastric bypass	Surgery: −8.85 kg/m^2 (−9.08 to −8.61)	Macroalbuminuria: HR, 0.55; 95% CI, (0.47 to 0.65) Severe kidney disease (HR, 0.50; 95% CI, 0.37 to 0.68) RRT (HR, 0.25; 95% CI, 0.08 to 0.72)
Shulman *et al.*[79] (IJO)	Matched prospective cohort study (SOS)/4047	eGFR: 92.4 (14.6)	Vertical band gastroplasty: 68.1% Gastric bypass: 13.2% Adjustable banding: 18.7%	No data	ESKD: overall: HR, 0.46 (95% CI, 0.24 to 0.90)
Coleman *et al.*[75] (United States)	Retrospective matched cohort/802 (surgery)	Stage 3–93.5% Stage 4–6.5% Proteinuria A2/A3—36.7%	Roux-en-Y gastric bypass-61%; sleeve gastrectomy—36% and adjustable gastric banding—3%	No data	Risk of mortality: HR, 0.21; 95% CI, 0.1 to 0.32
Kukla *et al.*[80] (United States)	Retrospective study/54 (SG group)	ESKD	Sleeve gastrectomy	Mean weight loss: 26.5 +/1 12.8 kg at 12-mo follow-up	Active listing: 37/54 DG patients versus 14/50 in the control group Kidney transplant: 20/54 patients versus 14/50 in the control group
Soliman *et al.*[81]	Retrospective study/MBS-AQIP 2011–2018 (*n*=38)	ESKD	Roux-en-Y gastric bypass—24 Laparoscopic sleeve gastrectomy—14	Mean weight loss (12 mo): 23.26 +/10.37 kg	Listed for transplant: 47% (*n*=18) Kidney transplant: 21% (*n*=8)
Aminian *et al.*[76]	425 patients	CKD progression, defined as decline of eGFR by ≥50% or to <15 ml/min per 1.73 m^2, initiation of dialysis, or kidney transplant	Surgery: 183 (RYGB: 54.1%; SG: 45.9%) GLP-1 RA: 242	Mean weight loss (8 yr): surgery 21.6% versus GLP-1 RA group 8.1% $P < 0.001$	Composite end point: favoring surgery 0.40 (95% CI, 0.21 to 0.76)

BMI, body mass index; CI, confidence interval; GLP-1 RA, glucagon-like protein-1 receptor agonist.

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Table 4. Kidney-specific metabolic/bariatric surgery checklist

Time Period	CKD Stage	
	1–5	5D
Immediate preoperatively		
Obtain baseline creatinine and UPCR/UACR	Yes	—
Consult nephrology on patients with preexisting kidney disease	Yes	Yes
Optimize fluid status, electrolytes, chemistries, hemoglobin	Yes	Yes
Early postoperative care		
Ensure adequate fluid intake	Yes	Yes
Monitor urine output	Yes	—
Monitor for rhabdomyolysis	Yes	—
Avoid medications that pose unnecessary kidney risk	Yes	—
Renally dose medications	Yes	Yes
Adjust hypertension and diabetes medications	Yes	Yes
Follow serum creatinine daily	Yes	—
Longer term follow-up		
Monitor for hyperoxaluria and kidney stone risk	Yes	—
Trend serum creatinine and proteinuria	Yes	—
Prompt referral to nephrology if serum creatinine rising	Yes	—
Follow bone mineral disease parameters	Yes	Yes
Monitor for vitamin D deficiency	Yes	Yes
Monitor for inadequate protein intake	Yes	Yes
Monitor mineral bone disease parameters	Yes	Yes
Avoid NSAIDs	Yes	—
Adjust hypertension and diabetes medications	Yes	Yes
Monitor for sarcopenia and frailty	Yes	Yes
Monitor for micro and macronutrient undernutrition	Yes	Yes

NSAID, nonsteroidal anti-inflammatory drug; UACR, urine albumin-creatinine ratio.

period is designed to minimize patient risk by watching for peri-perative complications, adjusting medications, and avoiding risks of AKI. Over the longer term, assessing patients for general and kidney-specific risks that may develop is recommended (Table 4). Because risk of oxalate nephropathy is higher in persons undergoing intestinal bypass, nonbypass procedures may be preferred for transplant-eligible candidates to prevent kidney oxalate deposition, but more research is needed to determine the best procedure. Furthermore, close monitoring for the risk of malnutrition (higher risk in those undergoing malabsorptive procedures) is recommended for all populations with kidney diseases, especially in those with advanced disease or on dialysis.

Implementation Considerations

Consideration of the barriers and facilitators to addressing obesity as an important adverse health risk for persons with kidney disease is essential for implementation of this KHG. Table 5 summarizes the ideal framework for the comprehensive management of persons living with obesity and kidney diseases. Although knowledge of obesity management is important, clinicians must also be willing to prescribe lifestyle modifications and weight loss medications and/or refer patients to metabolic and bariatric surgery centers. Clinicians must also consider local insurance coverage, cost, and patient support for initiation and maintenance of interventions. Prohibitive cost and lack of insurance coverage continue to limit access to the most effective weight loss medications, particularly for individuals from low-income and underprivileged communities. Currently, Medicare and Medicaid provide coverage only for semaglutide given subcutaneously to reduce the risk of heart attacks and stroke in people with cardiovascular disease who are overweight or obese.

Future Research and Policy Priorities

Although the evidence for appropriate management of obesity is expanding in patients living with kidney diseases, gaps in knowledge and implementation require attention. A team-based approach to weight management is preferred to ensure intensive, holistic treatment, but this is often not feasible because of limited clinical resources and lack of policies, payment models, and insurance coverage to encourage and prioritize comprehensive treatment. If possible, clinicians should collaborate with registered dietitians who have a certificate of training in obesity,[40] are a certified specialist in renal nutrition and/or obesity and weight management, or have completed other relevant continuing education or experience. Despite current coverage of medical nutrition therapy by most insurance providers, including Medicare, there is limited use of registered dietitians in the setting of kidney diseases. Collaboration with obesity medicine specialists and/or bariatric/metabolic surgeons may also be beneficial. The following key points provide an overview of important future research and policy priorities.

Research Priorities

- Define how changes in body composition affect the accuracy of GFR estimation.

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Table 5. Key practice points for the management of persons living with obesity and kidney disease

Psychosocial Assessment and Management
➢ Communicate with empathy and ask permission to discuss weight ➢ Screen for mood, anxiety, eating disorders, and substance misuse. Comprehensive nephrology clinics should have ready access to mental health professionals ➢ Screen for health-related social needs, involve social worker, and provide information on support services ➢ Assess for patient motivation and understanding of patient goals for weight loss ➢ Consider involvement of a multidisciplinary team and identify referral pathways to address psychosocial needs throughout treatment (management) process

Lifestyle Modifications	Special Considerations
➢ Frame weight management goals in terms of managing risk of kidney diseases and associated comorbidities ➢ Reflect each person's preferences, willingness, and ability to engage with available resources in weight loss approaches ➢ Refer to registered dietitians and exercise physiologists or trainers to encourage lifelong lifestyle modifications to achieve and maintain weight and behaviors that align with kidney health goals	Hemodialysis Assure adequate protein intake because of the high risk of PEW Peritoneal dialysis Account for glucose load when calculating daily calorie intake After transplant Discuss the risk of rapid weight gain after transplant Encourage gradual increase in exercise after transplant surgery

Pharmacologic Therapies	Special Considerations
➢ Gain proficiency in prescribing AOMs and monitoring use to ensure efficacy and safety in adults living with obesity and kidney diseases ➢ Consider eGFR, comorbidities, and unique barriers to weight loss (*e.g.*, cravings, portion control, insulin resistance, frailty) when prescribing AOMs ➢ Consider prescribing GLP-1 RAs or dual GLP-1 and GIP RAs for the most effective and beneficial outcomes ➢ Consider collaboration and communication with primary care and endocrinology clinicians when adjusting complex diabetes regimens for people with obesity, diabetes, and kidney diseases	Patients on insulin Monitor for hypoglycemia if on insulin and using GLP-1 Patients with ESKD Consider slower dose uptitration and achieving a lower maximum dose

Metabolic and Bariatric Surgery	Special Considerations
➢ Refer individuals with kidney disease and class 2 or class 3 obesity despite use of lifestyle modifications and/or AOMs to bariatric centers for further assessment of MBS ➢ Consider referral for either sleeve gastrectomy or gastric bypass as potential options in adults with obesity and kidney disease, depending on individual factors ➢ Monitor individuals with obesity and kidney diseases undergoing metabolic/bariatric surgery for increased risk of kidney stones and malnutrition, especially in those with advanced kidney disease ➢ Include a multidisciplinary care team both before and after metabolic/bariatric surgery to coordinate care and sustain weight loss	Kidney transplant candidates Sleeve gastrectomy may be preferred in kidney transplant candidates over gastric bypass to avoid negative effects on absorption of immunosuppression and oxalate absorption

AOM, antiobesity medication; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like protein-1 receptor agonist; PEW, protein energy wasting.

- Determine the effect of lifestyle modification interventions and AOMs in subgroups of patients living with kidney diseases and obesity including advanced stages of kidney disease, patients with kidney transplantation, and patients with frailty and sarcopenic obesity.
- Delineate whether combined lifestyle interventions, such as diet with exercise, is more effective than individual treatments.
- Establish whether the short- and midterm safety profile for AOMs in the general population generally reflects the safety profile in patients with stages 3–5 CKD, including ones on dialysis and with kidney transplantation. A diligent approach, including phase 4 studies, is necessary.
- Determine the cost-effectiveness of obesity management strategies in patients with kidney diseases.
- Perform economic analyses and modeling for cost–benefit and return on investment for single or combined weight management strategies to provide concrete data for policymakers to integrate these approaches in insurance plans.

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Policy Priorities

- Advocate for better insurance coverage and higher reimbursement rates across the care continuum. Additional innovative approaches, such as telenutrition and virtual visits, could be incorporated into the obesity management bundle.

Education Priorities

- Encourage adequate training, time, and interdisciplinary care teams to best facilitate comprehensive and sensitive conversations around weight management.
- Enhance obesity management training and education for nephrologists during fellowship and with continuing medical education.
- Develop and evaluate group education models that incorporate kidney diseases, diabetes, and obesity knowledge/skill building for patients.

Quality Improvement Priorities

- Develop toolkits to build, strengthen, and sustain multidisciplinary care teams (including registered dietitian, obesity medicine, physical therapy, and mental health providers).
- Create workflows to encourage integration of obesity assessment, discussions, and treatment into kidney disease treatment.

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Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/JSN/E858.

Supplemental Table 1. Health-related social needs screening resources and referral options.

Supplemental Table 2. Review of key studies on incretin mimetics.

Supplemental Table 3. General benefits and risks with various bariatric procedures.

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